

8EHQ-0103-15268



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Attention: TSCA Section 8(e) Coordinator

RE: Hydrotreated C5 – OECD 422 Study in Rats by Inhalation Exposure

Dear Sir or Madam:

The American Chemistry Council Olefins Panel submits this letter on behalf of certain of its members¹ pursuant to Section 8(e) of the Toxic Substances Control Act (TSCA) to inform EPA of preliminary histopathology results from an OECD 422 study that was conducted for Hydrotreated C5 in Sprague Dawley rats. The Panel has not made a determination as to whether a significant risk of injury to health or the environment is actually presented by the preliminary findings.

Hydrotreated C5 was tested pursuant to the Olefins Panel's testing plan for the C5 non-Cyclics Category under the High Production Volume Chemical Challenge Program.² The Hydrotreated C5 stream is a hydrotreated hydrocarbon fraction separated from pyrolysis gasoline that consists of substantial concentrations of pentenes, pentanes, and cyclopentene; a low amount of 2-methyl-2-butene ($\leq 11\%$) and isoprene (approximately 2%); and very small

¹ The sponsor companies are BP Amoco Chemical Company, Chevron Phillips Chemical Company LP, The Dow Chemical Company, Equistar Chemicals, LP, ExxonMobil Chemical Company, The Goodyear Tire & Rubber Company, Huntsman Corporation, NOVA Chemicals Inc. and Shell Chemical Company LP.

² The test plan is available at <http://www.epa.gov/chemrtk/olefins/olefintp.pdf>.

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amounts of other C5 dienes. CAS Registry numbers that are used by Panel members to identify Hydrotreated C5 streams include: 64742-49-0 (Naphtha, petroleum, hydrotreated light), 68410-97-9 (Distillates, petroleum, light distillate hydrotreating process, low-boiling), 68602-79-9 (Distillates, petroleum, benzene unit hydrotreated depentanizer overheads), and 68603-00-9 (Distillates, petroleum, thermal cracked naphtha, and gas oil).

The preliminary histopathology results of the 422 study were reported in a laboratory study update memorandum (attached) that described the findings for all (12/sex/group) control and high dose (8500 ppm) animals. Included in the findings were changes in the high dose group nasal turbinates with 3 male and 3 female rats showing minimal to slight atrophy/disorganization of the olfactory epithelium.

A final report is not available at this time but will be forwarded when received from the laboratory.

If you have any questions, please contact me at 301 924 2006 or Elizabeth_Moran@americanchemistry.com.

Yours truly,



Elizabeth J. Moran, Ph.D.
Manager, Olefins Panel

cc: Richard H. Hefter (MC 7403)

MICROSCOPIC PATHOLOGY

Terminal animals

Treatment-related findings for Air control groups and 8500 ppm exposure groups

Kidneys

An increase in the incidence and severity of hyaline droplets in cortical tubules was observed in all male rats exposed to 8500ppm Hydrotreated C5 compared to air control animals. In animals of both sexes exposed to 8500ppm Hydrotreated C5 an increase was noted in both the incidence and severity of basophilic cortical tubules.

		Male				Female					
Group		1	2	3	4	1	2	3	4		
Treatment		Air	Hydrotreated C5				Air	Hydrotreated C5			
Exposure conc. (ppm)		0	1000	3000	8500	0	1000	3000	8500		
Cortical tubules with hyaline droplets	Total	2			12c	0			0		
	Minimal	2			0	0			0		
	Slight	0			0	0			0		
	Moderate	0			7	0			0		
	Marked	0			5	0			0		
Number of kidneys examined		12			12	12			12		

c - $p < 0.001$ with Fisher's Exact Test, on total incidences only

		Male				Female					
Group		1	2	3	4	1	2	3	4		
Treatment		Air	Hydrotreated C5				Air	Hydrotreated C5			
Exposure conc. (ppm)		0	1000	3000	8500	0	1000	3000	8500		
Cortical tubular basophilia	Total	2			8a	0			4		
	Minimal	2			7	0			4		
	Slight	0			1	0			0		
Number of kidneys examined		12			12	12			12		

a- $p < 0.05$ with Fisher's Exact Test, on total incidences only

Liver

Minimal centrilobular hepatocyte hypertrophy was found only in some male rats in the air control group and 8500ppm Hydrotreated C5 exposure group, with an increased incidence in the latter animals.

		Male				Female					
Group		1	2	3	4	1	2	3	4		
Treatment		Air	Hydrotreated C5				Air	Hydrotreated C5			
Exposure conc. (ppm)		0	1000	3000	8500	0	1000	3000	8500		
Hepatocyte hypertrophy, centrilobular	Total	2			9a	0			0		
	Minimal	2			9	0			0		
Number of livers examined		12			12	12			12		

a- $p < 0.05$ with Fisher's Exact Test, on total incidences only

Nasal Turbinates

An increase in the incidence and severity of atrophy/disorganisation of the olfactory epithelium was observed in animals of both sexes exposed to 8500ppm Hydrotreated C5 compared to the air control animals.

		Male				Female					
Group		1	2	3	4	1	2	3	4		
Treatment		Air	Hydrotreated C5				Air	Hydrotreated C5			
Exposure conc. (ppm)		0	1000	3000	8500	0	1000	3000	8500		
Olfactory epithelium-atrophy/disorganisation	Total	0			3	0			3		
	Minimal	0			1	0			2		
	Slight	0			2	0			1		
Number of nasal turbinates examined		12			12	12			12		

Other Findings

In the spleen, a slightly higher incidence of extramedullary haemopoiesis was recorded in animals exposed to 8500ppm Hydrotreated C5 compared to air control animals. This is not considered related to treatment because of the natural variation in this physiological feature and the absence of treatment-related effects in the haematological parameters on comparing the groups.

Incidental findings

All other microscopic findings were considered to be incidental and of no toxicological importance.

Conclusion

The following treatment-related changes were observed following inhalation administration of Hydrotreated C5, via whole body exposure once daily for 6 hours, until the day prior to sacrifice in Study Week 5.

In male rats exposed to 8500ppm Hydrotreated C5, compared to air control males, renal cortical tubules with hyaline droplets were increased in incidence and severity. Basophilic cortical tubules were also increased in incidence and severity in the exposed group of both sexes.

In the liver, minimal centrilobular hepatocyte hypertrophy was found only in male rats in the air control group and 8500ppm exposure group, with an increased incidence in the latter group. This finding correlates with the increased bodyweight adjusted liver weights reported in the male 8500ppm exposure group.

In the nasal turbinates, atrophy/disorganisation of the olfactory epithelium was found in the male and female groups exposed to 8500ppm Hydrotreated C5. Although the incidences had not achieved statistical significance, it is considered that they are above background level and the finding is treatment-related.

Recommendation

In the light of the treatment-related findings it is recommended that histopathological examination of the kidneys, livers and nasal turbinates of the 1000ppm (Group 2) and 3000ppm (Group 3) exposed animals now be undertaken.

DRAFT

CSS/022

HYDROTREATED C5

4 WEEK GENERAL TOXICITY AND REPRODUCTION/DEVELOPMENT

TOXICITY SCREENING TEST BY INHALATION EXPOSURE TO RATS

(OECD 422 GUIDELINE)

DRAFT

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23 December 2002